UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,081	02/13/2006	Zhong Chao Yin	2577-160	6297

6449 7590 02/07/2007

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
ZHENG, LI	
ART UNIT	**PAPER NUMBER**
1638	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	02/07/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 02/07/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,081	YIN ET AL.	
	Examiner	Art Unit	
	Li Zheng	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11-13 and 19-34* is/are pending in the application.

4a) Of the above claim(s) *2,4,6-7,19-21,23-24,31-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,11-13,22 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 February 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5242006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1, 3, 5, 11-13, and 22, cancellation of claims 16 and 17, amendment to the claims, 3, 5, 11, and 19, as well as submission of new claims 25-34 in the reply filed on 11/13/2006 are acknowledged. Applicants also elected SEQ ID NO: 5 and 3. The new claims are entered, however, only claims 25-30 belong to elected invention group and are examined on the merits together with the claims in Group I. As a result, claims 1-8, 11-13, 19-34 are pending and claims 1, 3, 5, 11-13, 22 and 25-30 are examined on the merits. The Applicants argue that the technical feature, which is nucleotide sequence encoding SEQ ID NO: 5 or nucleotide sequence greater than about 50 bps that hybridizes under stringent condition to nucleotide sequence encoding SEQ ID NO: 5 and that confers resistance to Xanthomonas, is not anticipated by Zhang et al (response, page 7, 1st paragraph). The examiner disagrees. Since the stringent condition is not defined in the specification, any sequence including the ones of Zhang et al. could hybridizes to nucleotide sequence encoding SEQ ID NO: 5. Therefore, such technical feature does not constitute a special technical feature, which establishes that the inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1. Applicants are reminded that the examiner is required to further establish undue search burden under the PCT Rule.

The Applicants further traverse the restriction requirement regarding to sequence election (response, page 7, 2nd paragraph to page 9, 4th paragraph). First, Applicants are reminded that the requirement for sequence election is not to be construed as a requirement for an election of species, since each nucleotide and amino acid sequence is not a member of single genus of invention, but constitutes an independent and patentably distinct invention. However, in light of the Applicants' submission that SEQ ID NO: 1-4 all encode the same protein of SEQ ID NO: 5, the restriction requirement between SEQ ID NO: 1-4 is withdrawn. As a result, SEQ ID NO: 1-5 are elected sequences. Applicants are advised that since the restriction between SEQ ID NO: 1-4 is withdrawn, if any claim(s) that include(s) the limitation of the examined claims is/are presented in a continuation or divisional application, the claim of the application may be subject to a provisional statutory and/or nonstatutory double patenting rejection over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 no longer apply. MPEP804.01. The examiner, however, maintains other restriction requirements.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The hyperlinks shown on the specification page 22, line 11; page32, last line; and page 40, lines 3 and 6 need to be disabled.

3. The specification is objected to under 37 CFR 1.821(d) as failing to refer to a sequence by use of its sequence identifier preceded by "SEQ ID NO:". The nucleotide sequences in Figures 9 should be identified with SEQ ID NOs. Alternatively, the brief descriptions of those figures on page 5 can be amended to recite the identifiers.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 3, 5-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A review of the full content of the specification indicates that nucleotide sequences of greater than 50 bps which hybridize under stringent condition to nucleotide sequences encoding SEQ ID NO: 5 and provide a plant resistance to Xanthomonas, nucleotide sequences comprising at least 100 contiguous bps thereof that provide a plant resistance to Xanthomonas, as well as nucleotide sequences which hybridize under stringent condition to nucleotide sequences of SEQ ID NO: 1-4 and provide a plant resistance to Xanthomonas are essential to the instant invention.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." (See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

A review of the language of claims 1,3 and 22 indicates that claims are broadly drawn to a genus of nucleotide sequences of greater than 50 bps which hybridize under

stringent condition to nucleotide sequences encoding SEQ ID NO: 5 and provide a plant resistance to Xanthomonas, nucleotide sequences comprising at least 100 contiguous bps thereof that provide a plant resistance to Xanthomonas, as well as nucleotide sequences which hybridize under stringent condition to nucleotide sequences of SEQ ID NO: 1-4 and provide a plant resistance to Xanthomonas. However, neither the specification nor the prior art discloses any nucleotide sequences in claimed genus except for SEQ ID NO: 1-4, which all encode the same polypeptide of SEQ ID NO: 5. Further more, neither the specification nor the prior art teaches the essential structures of SEQ ID NO: 1 that are required for Xanthomonas resistance. The specification does not correlate the function of Xanthomonas resistance with any nucleotide sequences other than the SEQ ID NO: 1. Simply specifying what the sequence does without clearly specifying what the sequence is does not satisfy the written description requirement. Therefore, given the lack of enough description of the claimed genus, a person skilled in the art would conclude that applicants are not in possession of the claimed nucleotide sequences.

5. Claims 1, 3, 5, 11-13, 22 and 25-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleotide sequences or vector comprising the nucleotide sequence of SEQ ID NO: 1, does not reasonably provide enablement for SEQ ID NO: 2-4, any sequences encoding SEQ ID NO: 5, nucleotide sequences of greater than 50 bps which hybridize under stringent condition to nucleotide sequences encoding SEQ ID NO: 5 and provide a plant resistance to

Xanthomonas, nucleotide sequences comprising at least 100 contiguous bps thereof that provide a plant resistance to Xanthomonas, or nucleotide sequences which hybridize under stringent condition to nucleotide sequences of SEQ ID NO: 1-4 and provide a plant resistance to Xanthomonas. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The specification teaches that Xa31 gene from wild rice was show to be responsible for providing resistance to Xanthomonas to the hybrid rice strain (page 14-17). The specification further teaches that the Xa31 locus was mapped to a genetic interval of 146-kb between M3623 and 3612EST2 (page 23, last paragraph). The BAC clones were then identified and sequenced which generated a contig of 158,425 bps (page 25, 1st paragraph). In addition, genetic complementation was performed to isolate the Xa31 genomic clone. An overlapping region of 5198 bps was revealed (SEQ ID NO: 1) to be responsible for the complementation. The corresponding region from the recessive allele was also cloned as a 5131 bp fragment (SEQ ID NO: 2). The full-length cDNAs from resistance allele and recessive allele were also cloned (SEQ ID NO: 3 and 4, respectively), both of which encode the polypeptide of SEQ ID NO: 5. No other expressing regions within SEQ ID NO: 1 were identified. The comparisons of promoter regions of the gene encoding SEQ ID NO: 5 between resistance allele and recessive allele reveal several sequence differences. GFP tagging experiment further showed that functional terminators of said gene are identical between two alleles (paragraph [0087]). The specification concluded that SEQ ID NO: 1, 3, 4, and 5 are genomic clone, the

cDNA clone and deduced polypeptide sequence of Xa31 candidate. The coding regions of the Xa31 candidates were identical between resistance and recessive alleles. The Xa31 gene encodes a novel protein showing similarity at its C-terminal to rat or human NE1 protein. The regulation of expression of the Xa31 candidate gene might reside in the 5' upstream or 3' downstream region of the coding region (paragraph [0088].

However, the specification does not provide enough evidence to demonstrate that the polypeptide of SEQ ID NO: 5 is responsible for the resistance to Xanthomonas and therefore is the Xa31 gene. On the contrary, the specification seems teach away from it. First, the specification shows that the coding regions of the Xa31 candidates were identical between resistance and recessive alleles. Second, the specification teaches that the expression pattern of putative Xa31 gene are similar in resistant and susceptible lines (paragraph [0084]). Finally, the specification teaches that the functional terminator are identical between two alleles. The specification fails to demonstrate that SEQ ID NO: 5 is the protein responsible for providing the resistance. The only sequences enabled by the specification are the sequences comprising SEQ ID NO: 1. Without further guidance, undue experimentation would be required for a person skilled in the art to use the sequences encoding SEQ ID NO: 5 including SEQ ID NO: 2-4. See *Genentech Inc. v. Novo Nordisk,* A/S (CA FC) 42 USPQ2d 1001 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Further, even if the sequences encoding SEQ ID NO: 5 including SEQ ID NO: 2-4 were enabled, the specification still would not reasonably provide enablement for

nucleotide sequences of greater than 50 bps which hybridize under stringent condition to nucleotide sequences encoding SEQ ID NO: 5 and provide a plant resistance to Xanthomonas, nucleotide sequences comprising at least 100 contiguous bps thereof that provide a plant resistance to Xanthomonas, or nucleotide sequences which hybridize under stringent condition to nucleotide sequences of SEQ ID NO: 1-4 and provide a plant resistance to Xanthomonas. There is no guidance provided by the specification regarding to the functional motifs required for providing the Xanthomonas resistance. The only guidance provided by the specification is that the Xa31 gene encodes a novel protein showing similarity at its C-terminal to rat or human NE1 protein. The claims, however, are broadly drawn to any nucleotide sequences of greater than 50 bps which hybridize under stringent condition to nucleotide sequences encoding SEQ ID NO: 5 and provide a plant resistance to Xanthomonas, any nucleotide sequences comprising at least 100 contiguous bps thereof that provide a plant resistance to Xanthomonas, or any nucleotide sequences which hybridize under stringent condition to nucleotide sequences of SEQ ID NO: 1-4 and provide a plant resistance to Xanthomonas. First, As discussed above, since the stringent condition is not defined in the specification, any sequence could hybridizes to nucleotide sequence encoding SEQ ID NO: 5. Therefore, the claims read on any sequences that provide a plant resistance to Xanthomonas. The specification clear does not enable all of said sequences. Second, even if the stringent condition was defined properly, the state-of-the-art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or

nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674 bp fragment using a 497 bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99 bp insertion and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotides mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93 bp of DNA (page 862, Figure 2). In the present example, the isolated fragment of Frourgoux-Nicol et al exhibits less than 50% sequence identity with the probe to which the fragment hybridized. With the nucleotide sequences differ as much as 50%, the polypeptides encoded could be different from SEQ ID NO: 5. The specification provides no guidance as to how to modify the SEQ ID NO: 5 without affecting its Xanthomonas resistance function.

Falcon-Perez JM et al. (1999, *J Biol Chem.* 274:23584-90) teach that when twenty-two single amino acid substitutions or deletions were introduced into the nucleotide binding domains, the proposed regulatory domain, and the fourth cytoplasmic loop of the yeast cadmium factor (Ycf1p) vacuolar protein by site-directed mutagenesis, two conserved amino acid residues, Glu (709) and Asp (821), were found to be unnecessary for Ycf1p biogenesis and function. The instant specification fails to provide guidance for which amino acids of SEQ ID NO: 14 can be altered, the type of

alteration, and which amino acids must not be changed, to maintain DGAT activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al. (1988, Mol. Cell. Biol. 8:1247-1252) teach that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins would have at least 95% identity to the original protein.

Guo et al. (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing claimed nucleic acid sequences or proteins would require undue experimentation.

Given claim breadth, unpredictability of the art, and lack of guidance and additional working examples, undue experimentation would be required by one skilled in the art to practice the claimed invention in full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1,3, 5, 11-13, 22, 26-27, and 29-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (1999, *Nature Biotech*. 17:1021-1024).

Zhang et al. teach that transgenic sugarcane plants expressing an *albD* gene under the control of a constitutive promoter, maize ubi promoter, can confer a high level of resistance to symptom induction, and multiplication and systemic invasion by *Xanthomonas albilineans* (page 1021, the 3rd paragraph of the left column and the paragraph bridging the left column and the right column). As discussed above, since the stringent condition is not defined in the specification, any sequence could hybridizes to nucleotide sequence encoding SEQ ID NO: 5. Therefore, the claims read on any sequences that provide a plant resistance to Xanthomonas. In addition, in claim 5, the recitation, "the isolated nucleotide sequence encodes a polypeptide of SEQ ID NO: 5" (emphasis added), reads on any sequences encoding two residues of SEQ ID NO: 5. The reference therefore teaches all the limitation set forth by instant claims. However,

claims 5-8, 27-30 would obviate the rejection, should the recitation replaced with -- the isolated nucleotide sequence encodes the polypeptide of SEQ ID NO: 5 --.

7. Claims 1,3, 5,11-13, 22, 26-27, and 29-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Sasaki et al. (2001, GenBank Accession No. AP003623).

Sasaki et al. teach the sequence of a PAC clone: P0642B07 from rice chromosome 6. The nucleotides 105413-104934 matches 500 bps with SEQ ID NO: 3 and the putative polypeptide encoded has 84.5% identity to SEQ ID NO: 5. Given the sequence homology and the chromosomal location, the putative polypeptide is the corresponding gene of SEQ ID NO: 5 in japonica cultivar group. Therefore the putative polypeptide can inherently provide resistance to Xanthomonas. Given the homology at the nucleotide sequence level, the coding region is capable of hybridizing with the SEQ ID NO: 1-4. Since the whole gene is on a single PAC clone, the coding sequence and the its cognate plant promoter are cloned into a PAC vector. In addition, in claim 5, the recitation, "the isolated nucleotide sequence encodes a polypeptide of SEQ ID NO: 5" (emphasis added), reads on any sequences encoding two residues of SEQ ID NO: 5. The reference therefore teaches all the limitation set forth by instant claims. However, claims 5-8, 27-30 would obviate the rejection, should the recitation replaced with -- the isolated nucleotide sequence encodes the polypeptide of SEQ ID NO: 5 --.

Therefore, all the limitations are taught by the reference.

Conclusion

Claims 1, 3, 5, 11-13, 22 and 25-30 are rejected.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ELIZABETH MCELWAIN
PRIMARY EXAMINER